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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,573	02/26/2007	Daniel J. Smith	089498.0480.US	2362
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Joseph J. Crimaldi Roetzel & Andress 222 S. Main St. Akron, OH 44308			EXAMINER MARTINEZ, BRITTANY M	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/565,573

**Applicant(s)**

SMITH, DANIEL J.

**Examiner**

BRITTANY M. MARTINEZ

**Art Unit**

1793

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 January 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,4,6-9 and 11-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,6-9 and 11-25 is/are rejected.
- 7) ☒ Claim(s) 11,12 and 15-17 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 1/11/2010 and 3/5/2010
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Status of Application*

Applicant's arguments/remarks and amendments filed January 11, 2010, have been carefully considered. **Claims 1, 3, 4, 6-9 and 11-25** are pending in the instant application, with **Claims 1, 3, 4, 7, 13, 18, 21, 22 and 24** amended. **Claims 2, 5 and 10** have been cancelled. **Claims 1, 3, 4, 6-9 and 11-25** have been examined.

### *Abstract*

The abstract of the disclosure is objected to because "Ph" should be changed to "pH." Correction is required. See MPEP § 608.01(b).

### *Claim Objections*

1. **Claims 11, 12 and 15-17** are objected to because of the following informalities: **Claim 11** is dependent on cancelled claim, **Claim 10**. For examination purposes, it is assumed **Claim 11** is dependent on **Claim 7**. Appropriate correction is required.

### *Claim Rejections - 35 USC § 102/103*

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. **Claim 4** is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Abrams (US 2,844,546) (of record).
4. With regard to **Claim 4**, Abrams discloses a method for producing nitric oxide comprising producing nitric oxide by using a cationic exchange resin having a hydrogen-atom counter ion (Abrams, c. 7, l. 35-75; c. 8, l. 1-19 and 65-72).
5. **Claim 4** is also obvious over Abrams because anticipation is the epitome of obviousness.
6. **Claim 4** is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zhang et al. (*Electroanalysis* (newly cited)).
7. With regard to **Claim 4**, Zhang discloses a method for producing nitric oxide comprising producing nitric oxide by using a cationic exchange resin having a hydrogen-atom counter ion (Zhang, Abstract; p. 1113-1115).
8. **Claim 4** is also obvious over Zhang because anticipation is the epitome of obviousness.

9. **Claims 1 and 3** are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Batchelor et al. (US 2002/0115559 A1) (newly cited).
10. With regard to **Claims 1 and 3**, Batchelor discloses a method for producing nitric oxide comprising producing nitric oxide by using an anionic exchange resin having a nitrite counter ion (Batchelor, 0039-0041).
11. **Claims 1 and 3** are also obvious over Batchelor because anticipation is the epitome of obviousness.
12. **Claims 1, 3, 18, 19, 21, 22 and 24** are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Smith et al. (XP-002157493) (newly cited).
13. With regard to **Claims 1 and 3**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by using an anionic exchange resin having a diazeniumdiolate-containing composition counter ion (Smith, Abstract; p. 1151, "Synthesis of Polymers of Structure Type 3").
14. With regard to **Claims 18, 19 and 21**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanofiber (polyethylenamine fiber) having a diazeniumdiolate functional group (Smith, Abstract; p. 1150, c. 1; p. 1151, "Synthesis of Polymers of Structure Type 3" and "Synthesis of Polymers of Structure Type 4;" p. 1152).

15. With regard to **Claims 22 and 24**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanoparticle having a diazeniumdiolate functional group (Smith, Abstract; p. 1150, c. 1; p. 1151, "Synthesis of Polymers of Structure Type 3" and "Synthesis of Polymers of Structure Type 4;" p. 1152).

16. **Claims 1, 3, 18, 19, 21, 22 and 24** are also obvious over Smith because anticipation is the epitome of obviousness.

17. **Claims 1 and 3** are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Saavedra et al. (WO 98/13358) (newly cited).

18. With regard to **Claims 1 and 3**, Saavedra discloses a method for producing nitric oxide comprising producing nitric oxide by using an anionic exchange resin having a diazeniumdiolate-containing composition counter ion (Saavedra, Abstract; p. 25, l. 17 – p. 32, l. 30; Example 36).

19. **Claims 1 and 3** are also obvious over Saavedra because anticipation is the epitome of obviousness.

20. **Claims 1, 3, 6, 7, 11, 12, 18 and 21-24** are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II").

21. With regard to **Claims 1 and 3**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by using an anionic exchange resin having a diazeniumdiolate-containing composition counter ion (Saavedra II, Abstract; p. 8, l. 3-p. 11, l. 23; p. 17, l. 13-p. 18, l. 4; p. 19, l. 17-p. 21, l. 9).
22. With regard to **Claim 6**, Saavedra II discloses the anionic exchange resin in a gel (Saavedra II, p. 17, l. 13-20).
23. With regard to **Claims 7, 11 and 12**, Saavedra II discloses a method for producing nitric oxide comprising mixing a salt with a gel to produce nitric oxide, wherein the gel has an anionic exchange resin having a diazeniumdiolate-containing composition counter ion therein (Saavedra II, Example IV).
24. With regard to **Claims 18 and 21**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanofiber having a diazeniumdiolate functional group (Saavedra II, Abstract; p. 8, l. 3-p. 11, l. 23; p. 17, l. 13-p. 18, l. 4; p. 19, l. 17-p. 21, l. 9; p. 23, l. 10-19).
25. With regard to **Claims 22-24**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanoparticle (polystyrene) having a diazeniumdiolate functional group (Saavedra II, Abstract; p. 8, l. 3-p. 11, l. 23; p. 17, l. 13-p. 18, l. 4; p. 19, l. 17-p. 21, l. 9; p. 23, l. 10-19).
26. **Claims 1, 3, 6, 7, 11, 12, 18 and 21-24** are also obvious over Saavedra II because anticipation is the epitome of obviousness.

27. **Claims 18, 19, 22 and 23** are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Smith et al. (US 5,519,020) (newly cited).
28. With regard to **Claims 18 and 19**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding a pH adjuster to a nanofiber (polyethylenimine fiber) having a diazeniumdiolate functional group (Smith, Abstract; Claims 6-10; c. 3-c. 13).
29. With regard to **Claims 22 and 23**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding a pH adjuster to a nanoparticle (cellulose) having a diazeniumdiolate functional group (Smith, Abstract; Claims 6-10; c. 3-c. 13).
30. **Claims 18, 19, 22 and 23** are also obvious over Smith because anticipation is the epitome of obviousness.

***Claim Rejections - 35 USC § 103***

31. **Claims 8 and 9** are rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II") as applied to **Claim 7** above, and further in view of Fine et al. (US 2003/0064028 A1) (of record).
32. Saavedra II does not disclose the salt being sodium chloride, sodium phosphate, or sodium acetate (**Claim 8**); nor the gel being an ion-free hydrogel (**Claim 9**).
33. With regard to **Claims 8 and 9**, Fine discloses a method for producing nitric oxide comprising the step of mixing a salt (sodium chloride) with a gel (ion-free



hydrogel) to produce nitric oxide, wherein the gel has a matrix therein (Fine, 0008, 0009, 0017, 0018, 0025, 0038, 0040, 0041, Examples 1 and 2; Claims 1-8 and 16-18).

34. Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Saavedra II with the salt and hydrogel of Fine in order to obtain a process capable of precisely delivering nitric oxide at therapeutic levels (Fine, 0004; 0007-0008).

35. **Claims 7, 13 and 14** are rejected under 35 U.S.C. 103(a) as being unpatentable over Abrams (US 2,844,546) (of record) in view of Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II").

36. With regard to **Claims 7, 13 and 14**, Abrams discloses a method for producing nitric oxide comprising producing nitric oxide by using a cationic exchange resin having a hydrogen-atom counter ion (Abrams, c. 7, l. 35-75; c. 8, l. 1-19 and 65-72). The difference between the process of Abrams and that of **Claim 7** is Abrams does not disclose mixing a salt with a gel to produce nitric oxide, wherein the gel contains the ionic exchange resin therein.

37. With regard to **Claim 7**, Saavedra II discloses a method for producing nitric oxide comprising mixing a salt with a gel to produce nitric oxide, wherein the gel has an ionic exchange resin therein (Saavedra II, Example IV).

38. Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Abrams with the process of Saavedra II in order to obtain a process capable of producing pharmaceutical compositions that release nitric oxide at therapeutic levels (Saavedra II, Abstract).

39. **Claims 7, 13 and 14** are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (*Electroanalysis*) (newly cited) in view of Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II").

40. With regard to **Claims 7, 13 and 14**, Zhang discloses a method for producing nitric oxide comprising producing nitric oxide by using a cationic exchange resin having a hydrogen-atom counter ion (Zhang, Abstract; p. 1113-1115). The difference between the process of Zhang and that of **Claim 7** is Zhang does not disclose mixing a salt with a gel to produce nitric oxide, wherein the gel contains the ionic exchange resin therein.

41. With regard to **Claim 7**, Saavedra II discloses a method for producing nitric oxide comprising mixing a salt with a gel to produce nitric oxide, wherein the gel has an ionic exchange resin therein (Saavedra II, Example IV).

42. Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Zhang with the process of Saavedra II in order to obtain a process capable of producing pharmaceutical compositions that release nitric oxide at therapeutic levels (Saavedra II, Abstract).

43. **Claim 15** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Tucker et al. (US 2005/0036949 A1) (newly cited).

44. Saavedra does not disclose reacting a hydrogen-atom cation with ascorbate to produce ascorbic acid (**Claim 15**). However, Tucker discloses that ascorbic acid releases nitric oxide for pharmaceutical use (Tucker, Abstract; 0010; 0079). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Saavedra with the ascorbic acid of Tucker in order to release the nitric oxide.

45. **Claim 16** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Benjamin et al. (US 2002/0136750 A1) (newly cited).

46. Saavedra does not disclose reacting ascorbic acid with nitrite to form nitric oxide (**Claim 16**). However, Benjamin discloses that reacting ascorbic acid with nitrite releases nitric oxide for pharmaceutical use (Benjamin, Abstract; 0111). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Saavedra with the ascorbic acid/nitrite reaction of Benjamin in order to release the nitric oxide.

47. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Smith et al. (US 5,519,020) (newly cited).

48. Saavedra does not disclose reacting a hydrogen cation with the diazeniumdiolate-containing composition to produce nitric oxide (**Claim 17**). However,

Smith discloses that all that is required to release nitric oxide from a diazeniumdiolate-containing composition is a source of hydrogen cation (Smith, c. 10, l. 62-67). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Saavedra with the diazeniumdiolate-containing composition/hydrogen reaction of Smith in order to release the nitric oxide.

49. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (XP-002157493) (newly cited) as applied to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1) (newly cited).

50. Smith does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

51. With regard to **Claims 20 and 25**, Ignatious discloses an electrospun pharmaceutical composition comprising an electrospun fiber of a pharmaceutically acceptable polymeric carrier integrated with a pharmaceutically acceptable active agent (nanoparticle), wherein the composition achieves maximum bioavailability of a drug moiety (Ignatious, Abstract; Claims 1 and 2). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Smith with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

52. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (newly cited) (hereinafter, "Saavedra II") as applied

to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1) (newly cited).

53. Saavedra does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

54. With regard to **Claims 20 and 25**, Ignatious discloses an electrospun pharmaceutical composition comprising an electrospun fiber of a pharmaceutically acceptable polymeric carrier integrated with a pharmaceutically acceptable active agent (nanoparticle), wherein the composition achieves maximum bioavailability of a drug moiety (Ignatious, Abstract; Claims 1 and 2). Thus, it would have been obvious to one of ordinary skill in the art to modify the process of Saavedra with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

55. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 5,519,020) (newly cited) as applied to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1) (newly cited).

56. Smith does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

57. With regard to **Claims 20 and 25**, Ignatious discloses an electrospun pharmaceutical composition comprising an electrospun fiber of a pharmaceutically acceptable polymeric carrier integrated with a pharmaceutically acceptable active agent (nanoparticle), wherein the composition achieves maximum bioavailability of a drug moiety (Ignatious, Abstract; Claims 1 and 2). Thus, it would have been obvious to one

of ordinary skill in the art to modify the process of Smith with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

### ***Additional Prior Art***

The following prior art references are also relevant to the instant application, and could be used to reject the instant Claims:

- Donovan et al., "Quantification of Diazeniumdiolate Mutagenicity in Four Different *in Vitro* Assays," 1997, *Nitric Oxide: Biology and Chemistry*, Vol. 1, No. 2, pp. 158-166.
- Bivalacqua et al., "Analysis of Vasodilator Responses to Novel Nitric Oxide Donors in the Hindquarters Vascular Bed of the Cat," 2001, *Journal of Cardiovascular Pharmacology*, 38, pp. 120-129.
- Keefer et al., "Chemistry of the Diazeniumdiolates," 2001, *Nitric Oxide: Biology and Chemistry*, Vol. 5, No. 4, pp. 377-394.
- Keefer, "PROGRESS TOWARD CLINICAL APPLICATION OF THE NITRIC OXIDE-RELEASING DIAZENIUMDIOLATES," 2003, *Annu. Rev. Pharmacol. Toxicol.*, 43, pp. 585-607.
- Stinson et al., "Plasma pharmacokinetics of a liver-selective nitric oxide-donating diazeniumdiolate in the male C57BL/6 mouse," 2002, *xenobiotica*, Vol. 32, No. 4, pp. 339-347.
- Witt et al., "Comparison of responses to novel nitric oxide donors in the feline pulmonary vascular bed," 2001, *European Journal of Pharmacology*, 430, pp. 311-315.
- Arnold et al., "A Nitric Oxide-Releasing Polydiazeniumdiolate Derived from Acetonitrile," 2002, *Organic Letters*, Vol. 4, No. 8, pp. 1323-1325.
- Arnold et al., "Mechanistic insight into exclusive nitric oxide recovery from a carbon-bound diazeniumdiolate," 2002, *Nitric Oxide: Biology and Chemistry*, 7, pp. 103-108.
- Davies et al., "Chemistry of the Diazeniumdiolates. 2. Kinetics and Mechanism of Dissociation to Nitric Oxide in Aqueous Solution," 2001, *J. Am. Chem. Soc.* 123, pp. 5473-5481.

- Fitzhugh et al., "DIAZENIUMDIOLATES: PRO- AND ANTIOXIDANT APPLICATIONS OF THE 'NONOates,'" 2000, *Free Radical Biology & Medicine*, Vol. 28, No. 10, pp. 1463-1469.
- Furchgott, "Endothelium-Derived Relaxing Factor: Discovery, Early Studies, and Identification as Nitric Oxide," 1999, *Bioscience Reports*, Vol. 19, No. 4, pp. 235-251.
- Hrabie et al., "Conversion of Proteins to Diazeniumdiolate-Based Nitric Oxide Donors," 1999, *Bioconjugate Chem.*, 10, pp. 838-842.
- Hrabie et al., "Reaction of Nitric Oxide at the  $\alpha$ -Carbon of Enamines. A New Method of Preparing Compounds Containing the Diazeniumdiolate Functional Group," 2000, *J. Org. Chem.*, 65, pp. 5745-5751.
- Hrabie et al., "Chemistry of the Nitric Oxide-Releasing Diazeniumdiolate ("Nitrosohydroxylamine") Functional Group and Its Oxygen-Substituted Derivatives," 2002, *Chem. Rev.*, 102, pp. 11351154.
- Keynes et al., "Superoxide-dependent consumption of nitric oxide in biological media may confound in vitro experiments," 2003, *Biochem. J.*, 369, pp. 399-406.
- Mowery et al., "Preparation and characterization of hydrophobic polymeric films that are thromboresistant via nitric oxide release," 2000, *Biomaterials*, 21, pp. 9-21.
- Saavedra et al., "Targeting Nitric Oxide (NO) Delivery *in Vivo*. Design of a Liver-Selective NO Donor Prodrug That Blocks Tumor Necrosis Factor- $\alpha$ -Induced Apoptosis and Toxicity in the Liver," 1997, *J. Med. Chem.*, 40, pp. 1947-1954.
- Shami et al., "JS-K, a Glutathione/Glutathione S-Transferase-activated Nitric Oxide Donor of the Diazeniumdiolate Class with Potent Antineoplastic Activity," 2003, *Molecular Cancer Therapeutics*, Vol. 2, pp. 409-417.
- Saavedra et al., "Localizing Antithrombotic and Vasodilatory Activity with a Novel, Ultrafast Nitric Oxide Donor," 1996, *J. Med. Chem.*, 39, pp. 4361-4365.
- Saavedra et al., "The Secondary Amine/Nitric Oxide Complex Ion  $R_2N[N(O)NO]^-$  as Nucleophile and Leaving Group in  $SNAr$  Reactions," 2001, *J. Org. Chem.*, 66, pp. 3090-3098.
- Saavedra et al., "Conversion of a Polysaccharide to Nitric Oxide-Releasing Form. Dual-Mechanism Anticoagulant Activity of Diazeniumdiolated Heparin," 2000, *Bioorganic & Medicinal Chemistry Letters*, 10, pp. 751-753.
- Saavedra et al., "Esterase-Sensitive Nitric Oxide Donors of the Diazeniumdiolate Family: In Vitro Antileukemic Activity," 2000, *J. Med. Chem.*, 43, pp. 261-269.

### ***Response to Amendment***

Applicant's amendments filed January 11, 2010, with regard to the Abstract, Specification, Claims, and Oath/Declaration have been fully considered and are accepted. The objections to the Specification and Oath/Declaration of the previous Office action are withdrawn. It is noted that the Abstract remains objected to, as seen above.

### ***Response to Arguments***

58. Applicant's arguments with respect to the prior art rejections of the previous Office action have been considered but are moot in view of the new ground(s) of rejection. It is highly recommended that Applicant considers the references listed under "Additional Prior Art" when amending the instant claims as these references are relevant to the instant Claims and could be used in prior art rejections. It is further suggested that, in the interest of disclosure, Applicant submit and/or disclose all prior art references/publications with regard to his own work (non-patent literature, U.S. patent literature, and foreign patent literature).

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRITTANY M. MARTINEZ whose telephone number is



(571) 270-3586. The examiner can normally be reached on Monday-Friday 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stanley Silverman can be reached at (571) 272-1358. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wayne Langel/  
Primary Examiner, Art Unit 1793

BMM  
/Brittany M Martinez/  
Examiner, Art Unit 1793